Pyle disease

Pyle disease is a disorder of the bones. Its hallmark feature is an abnormality of the long bones in the arms and legs in which the ends (metaphyses) of the bones are abnormally broad; the shape of the bones resembles a boat oar or paddle. The broad metaphyses are due to enlargement of the spongy inner layer of bone (trabecular bone). Although trabecular bone is expanded, the dense outermost layer of bone (cortical bone) is thinner than normal. As a result, the bones are fragile and fracture easily. The bone abnormalities in the legs commonly cause knock knees (genu valgum) in affected individuals.

Other bone abnormalities can also occur in Pyle disease. Affected individuals may have widened collar bones (clavicles), ribs, or bones in the fingers and hands. Dental problems are common in Pyle disease, including delayed appearance (eruption) of permanent teeth and misalignment of the top and bottom teeth (malocclusion).

Frequency

Pyle disease is thought to be a rare disorder, although its prevalence is unknown. More than 25 cases have been described in the medical literature.

Genetic Changes

Pyle disease is caused by mutations in the *SFRP4* gene. This gene provides instructions for making a protein that blocks (inhibits) a process called Wnt signaling, which is involved in the development of several tissues and organs throughout the body. In particular, regulation of Wnt signaling by the SFRP4 protein is critical for normal bone development and remodeling. Bone remodeling is a normal process in which old bone is broken down and new bone is created to replace it. Mutations in the *SFRP4* gene are thought to prevent the production of functional SFRP4 protein. The resulting dysregulation of Wnt signaling leads to the bone abnormalities characteristic of Pyle disease.

Inheritance Pattern

Pyle disease is inherited in an autosomal recessive pattern, which means both copies of the *SFRP4* gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene. While they do not develop the condition, they may have mild abnormalities of the long bones.

Other Names for This Condition

- metaphyseal dysplasia, Pyle type
- Pyle metaphyseal dysplasia
- Pyle's disease
- Pyle's metaphyseal dysplasia syndrome

Diagnosis & Management

Genetic Testing

- Genetic Testing Registry: Pyle metaphyseal dysplasia
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0265294/

General Information from MedlinePlus

- Diagnostic Tests
  https://medlineplus.gov/diagnostictests.html
- Drug Therapy
  https://medlineplus.gov/drugtherapy.html
- Genetic Counseling
  https://medlineplus.gov/geneticcounseling.html
- Palliative Care
  https://medlineplus.gov/palliativecare.html
- Surgery and Rehabilitation
  https://medlineplus.gov/surgeryandrehabilitation.html

Additional Information & Resources

MedlinePlus

- Health Topic: Bone Diseases
  https://medlineplus.gov/bonediseases.html

Genetic and Rare Diseases Information Center

- Pyle disease
  https://rarediseases.info.nih.gov/diseases/4612/pyle-disease

Additional NIH Resources

- National Institute of Arthritis and Musculoskeletal and Skin Diseases: What Is
  Bone?
  https://www.niams.nih.gov/Health_Info/Bone/Bone_Health/default.asp

Educational Resources

- Disease InfoSearch: Pyle disease
  http://www.diseaseinfosearch.org/Pyle+disease/6110

- Merck Manual Consumer Version: Bones
  http://www.merckmanuals.com/home/bone,-joint,-and-muscle-disorders/biology-of-the-musculoskeletal-system/bones

- Orphanet: Pyle disease
  http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=3005

Patient Support and Advocacy Resources

- International Osteoporosis Foundation
  https://www.iofbonehealth.org/osteoporosis-musculoskeletal-disorders/skeletal-rare-disorders

- Little People of America: Skeletal Dysplasia Clinics
  http://www.lpaonline.org/regional-skeletal-dysplasia-clinics

- University of California Los Angeles: International Skeletal Dysplasia Registry
  http://ortho.ucla.edu/isdr

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28Pyle+disease%5BTIAB%5D%29+OR+%28Pyle's+disease%5BTIAB%5D%29+OR+%28Pyle+metaphyseal+dysplasia%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D

OMIM

- PYLE DISEASE
  http://omim.org/entry/265900

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